

Stanley I. Music, MD, DTPH, FACPM
The Greatest Vaccine Success: The Smallpox Eradication Story
National Center for Disease Control, Tbilisi, Rep. of Georgia, 2011-06-14

The Greatest Vaccine Success...



... the Smallpox Eradication Story

S Music

NCDC Tbilisi, June 14, 2011

**THE PRINCIPLES AND
PRACTICE OF MEDICINE**

DESIGNED FOR THE USE OF PRACTITIONERS
AND STUDENTS OF MEDICINE

BY
WILLIAM OSLER, M. D.

FELLOW OF THE ROYAL SOCIETY; FELLOW OF THE ROYAL COLLEGE OF PHYSICIANS,
LONDON; SENIOR PROFESSOR OF MEDICINE, OXFORD UNIVERSITY; HONORARY PRO-
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SIXTH EDITION, THOROUGHLY REVISED
FROM NEW PLATES



NEW YORK AND LONDON
D. APPLETON AND COMPANY
1907

"...The disease smoulders here and there in different localities, and when conditions are favorable becomes epidemic. This was well illustrated by the celebrated Montreal outbreak of 1885. For several years there had been no small-pox in the city, and a large unprotected population grew up among the French-Canadians, many of whom were opposed to vaccination. On February 28, a Pullman-car conductor, who had traveled from Chicago, where the disease had been slightly prevalent, was admitted into the Hôtel-Dieu, the civic small-pox hospital being at the time closed. Isolation was not carried out, and on the 1st of April a servant in the hospital died of small-pox. Following her decease, with a negligence absolutely criminal, the authorities of the hospital dismissed all patients presenting no symptoms of contagion, who could go home. The disease spread like fire in dry grass, and within nine months there died in the city of small-pox 3,164 persons..."

Quote from Osler's 1907 text, *Practice of Medicine*, page 113:

**ISOLATION
(QUARANTINE)
SMALLPOX**

No one shall enter or leave these premises except as provided in the Rules and Regulations of the State Department of Health or Local Board of Health.

IT IS A MISDEMEANOR PUNISHABLE BY LAW:

(1) To expose minor children to this Disease. (2) For any suscep-
tible child to return to school from these premises while this card
is posted. (3) To remove this placard without authority of the
Local Board of Health.

This card constitutes the official notice of the establishment of Isolation.

2
Health Officer

**Table 2. Peak Industrial Production of Dry Biowarfare
Agents, in Metric Tons* per Year, US**

Dry Biowarfare Agents	USA
Staphylococcal enterotoxin B	1.9
<i>E. tularensis</i> (tularemia)	1.6
<i>Coxiella burnetii</i> (Q fever)	1.1
<i>B. anthracis</i> (anthrax)	0.9
Venezuelan equine encephalitis	0.8
botulinum	0.2
<i>Yersinia pestis</i> (plague)	0
variola virus (smallpox)	0
<i>Actinobacillus mallei</i> (glanders)	0
Marburg virus	0
Total	6.5

* One metric ton equals 1,000 kilograms

Adapted from *Germs: Biological Weapons and America's Secret War*
Miller, Engelberg and Broad, 2001 Simon and Schuster, page 234

**Table 2. Peak Industrial Production of Dry Biowarfare
Agents, in Metric Tons* per Year, US versus USSR**

Dry Biowarfare Agents	USA	USSR
Staphylococcal enterotoxin B	1.9	0
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<i>Coxiella burnetii</i> (Q fever)	1.1	0
<i>B. anthracis</i> (anthrax)	0.9	4,500
Venezuelan equine encephalitis	0.8	150
botulinum	0.2	0
<i>Yersinia pestis</i> (plague)	0	1,500
variola virus (smallpox)	0	100
<i>Actinobacillus mallei</i> (glanders)	0	2,000
Marburg virus	0	250
Total	6.5	10,000

* One metric ton equals 1,000 kilograms

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Airborne Transmission of Smallpox, Meschede Hospital, Germany, 1970. Source: Fenner; Wehrle et al.

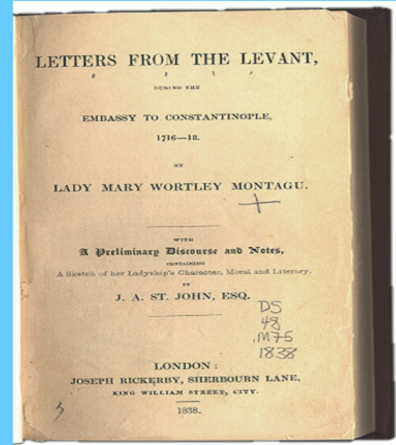
Meschede, Federal Republic of Germany 1970

The patient's room was on the first floor of the hospital. He had smallpox. Rooms were heated by radiators, and ventilation was provided by opening doors and windows. **Multiple secondary cases of smallpox occurred in staff, patients, and even visitors; some of whom were never on the floor where the index patient was housed.** Later, the air circulation was studied by smoke pattern, with a smoke source placed in the index case's room. Smoke traveled up the staircase to the second and third floors and out the windows and back inside, generally mirroring the distribution of cases that resulted. This provides strong evidence that smallpox was spread by the airborne route.

Variolation

"...In the middle of the sixteenth century, over 200 years before Jenner's epoch-making discovery, a form of inoculation against smallpox consisting of extracting and drying the contents of a pustule from a smallpox victim and blowing the powder into the nose, gained wide acceptance in China. Russian doctors came to China to study this method in the seventeenth century and news of it reached England in 1717..."

Away With All Pests
An English Surgeon in People's China: 1954-1969
 Dr. Joshua S. Horn



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President Thomas Jefferson wrote a letter to Jenner in 1806, focusing on the practical implications of vaccination, stating in part:

“...Medicine has never before produced any single improvement of such utility. Harvey's discovery of the circulation of the blood was a beautiful addition to our knowledge of the animal economy, but on a review of the practice of medicine before and since that epoch, I do not see any great amelioration which has been derived from that discovery. You have erased from the calendar of human afflictions one of its greatest. Yours is the comfortable reflection that mankind can never forget that you have lived. Future nations will know by history only that the loathsome small-pox has existed and by you has been extirpated...”

From a letter to Dr. Edward Jenner on his discovery of the smallpox vaccine, May 14, 1806

Important Dates in the History of Smallpox (adapted from Gross and Sepkowitz, 1998)

Date	Event
300	Earliest reported Chinese description of smallpox
679	Earliest specific European references to epidemic smallpox
10 th C.	Chinese physicians inoculate smallpox intranasally to create or enhance protection
1701	Chinese practice of subcutaneous inoculation relayed to Royal Society; meager interest generated
1716	Lady Wortley Montagu witnesses inoculation while resident in Turkey; has her children inoculated
1721	Lady Wortley Montagu introduces inoculation in England; generates interest among upper class; well publicized early fatalities sharply limit the growth of this practice
	Smallpox strikes Boston; Cotton Mather initiates controversial inoculation program
1757	Edward Jenner is inoculated safely (age 8 years)
1774	Benjamin Jesty vaccinates his children with cowpox matter; confirms exposure immunity smallpox
1775	George Washington orders all troops inoculated
1796	Edward Jenner vaccinates James Phipps with cowpox matter
1798	Jenner publishes “An Inquiry into the Causes and Effects of Variolæ Vaccinæ
1800	Benjamin Waterhouse uses Jenner vaccine in the United States
1967	WHO begins global initiative for the eradication of smallpox
1977	All Mao Maalin is the last human to contract naturally-acquired wild smallpox
1979	WHO decrees smallpox eradicated

Smallpox: The Disease Through 1973 Eyes

- relatively long incubation period (12-14 days)
- slow person-to-person spread from infectious cases, usually over 3 weeks (earliest skin lesions to the disappearance of all scabs)
- almost all cases display characteristic eruption, develops and evolves over 3 weeks (earliest skin lesions to the disappearance of all scabs)
- cases infectious only during rash, infectivity drops sharply after week #1
- inapparent infections extremely rare, not infectious
- infectious cases
 - readily identified on inspection without laboratory support
 - the only reservoir for the disease
- susceptibility is universal
- permanent immunity usually follows recovery from the disease
- second attacks are extremely rare and, when they occur, are (almost) always* milder than the first episode in that person
- no known effective treatment

* quote from Hopps

Smallpox: The Vaccine Through 1973 Eyes...

- a vaccine generally considered safe and very effective vaccine existed
 - easily transported
 - required no refrigeration
 - inoculated with a cheap unsterile device - the bifurcated needle
 - under tropical field conditions, >95% of vaccinees were completely protected for a minimum of 1 year after a single dose
 - immunity induced in only 7-10 days in persons never previously vaccinated
 - in fewer days in persons with past vaccination
 - routinely possible to abort an incubating infection in an exposed individual if vaccination is given within 4 to 5 days after exposure

Die Achphenomenon (1 of 2)

- At some point, probably in the early 1970's, it was realized that the strategy of mass vaccination which had worked to free Europe and much of the developed world from smallpox, was not going to work in places like India, Pakistan and Bangladesh
- There were too many people crowded into too small a geography
- Bangladesh, for example, had 10,000 new susceptibles born each day

Die Achphenomenon (2 of 2)

- Transmission, ongoing for many centuries, simply could not be interrupted without unachievable coverage (>99.99%)
- Understanding the epidemiology, however, led to the development of a strategy of surveillance and containment



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Smallpox: The Epidemiology (1 of 2)

- a focal disease of only moderate communicability, usually
- infectious cases comprise only a fraction of the population of an infected community
- only a fraction of communities in an infected country contain infectious cases at any one time
- the only persons at risk of acquiring smallpox are those susceptible individuals in actual physical contact with active cases or their fomites, usually
- there are no other hosts (reservoir) and there is no carrier state

Hence the strategy:

Surveillance

- find the active cases (using mobile surveillance teams, paying rewards for information re the location of infected villages, etc.)

Quarantine

Containment (ring vaccination)

- vaccinate all persons in the identified villages, maintain forced isolation for 2 incubation periods after last onset date
 - nobody gets in without a vaccination
 - nobody gets out if they have a rash

Smallpox: The Epidemiology (2 of 2)

- each time an active case is surrounded by a ring of freshly immunized non-susceptibles, a potential chain of infection is broken
- when such action is pursued at a faster rate than the natural transmission rate, the incidence of smallpox declines
- eradication occurs when the last case is so surrounded, when the chain of infection that has lasted so long is interrupted:

- Ramses V died 1157 B.C.
- Emperor Gokwomyo of Japan died 1654
- Queen Mary II of England died 1694
- King Louis XV of France died 1774
- Emperor Komei of Japan died 1867
- President Abraham Lincoln came down with smallpox a few hours after giving the Gettysburg Address, then sequestered himself in the White House with no visitors, no appointments, and no explanation until he recovered

The Basics of Smallpox Eradication

- 1 **Surveillance and Quarantine** to find the cases
- 2 **Containment** to interrupt transmission

The Smallpox Vaccine We Used: Its Safety Profile*

Adverse Event	Rate
Inadvertent inoculation	529.2/million primary vaccinations
Generalized vaccinia	245.1 per million primary vaccinations
Eczema vaccinatum	38.5 per million vaccinations
Progressive vaccinia	1.5 per million primary vaccinations
Post-vaccinal encephalitis	12.3 per million primary vaccinations
Death	~ 1 per million primary vaccinations

*Source: from a 1968 survey of 10 states, discussed in the
Interim Smallpox Response Plan & Guidelines, CDC, 2001

Smallpox Vaccine Reactions Jolt Experts; From Rashes to Fevers, Array of Side Effects Is Uncommon Today*

As physical specimens, the Baylor University students were fit and healthy, the "creme de la creme," in the words of researcher Kathy Edwards. Yet when she inoculated them with smallpox vaccine, arms swelled, temperatures spiked and panic spread.

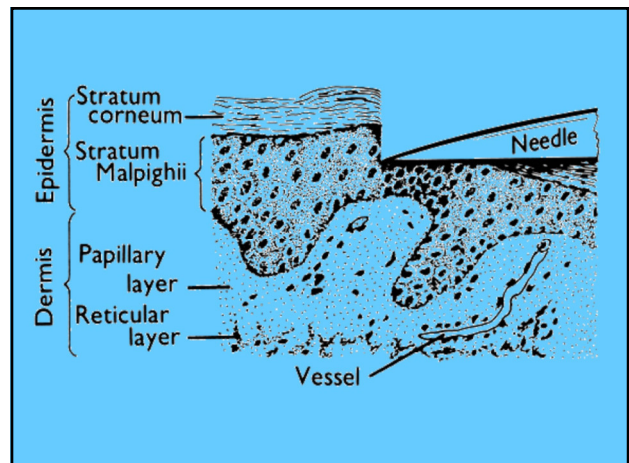
It was the same at clinics in Iowa, Tennessee and California. Of 200 young adults who received the vaccine as part of a recent government study, one-third missed at least one day of work or school, 75 had high fevers, and several were put on antibiotics because physicians worried that their blisters signaled a bacterial infection.

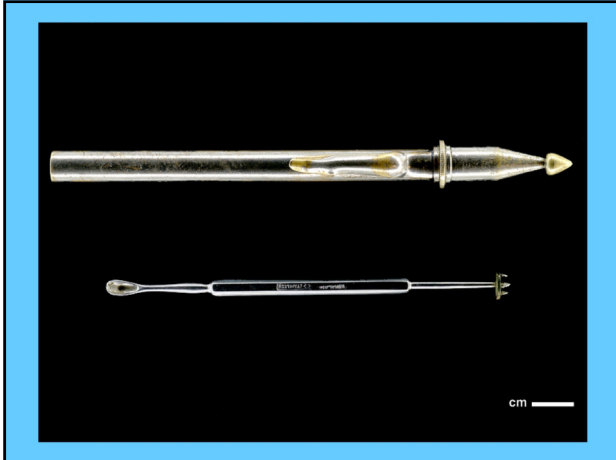
Even for experts such as Edwards, the Vanderbilt University physician overseeing the study, the side effects were startling. "I can read all day about it, but seeing it is quite impressive," she said. "The reactions we saw were really quite remarkable."

President Bush is poised to announce plans, perhaps as early as this week, to resume vaccinating Americans against smallpox as part of a massive push to protect the nation from a biological assault. As he weighs the decision, researchers are becoming reacquainted with the unpleasant — often severe — complications of the vaccine.

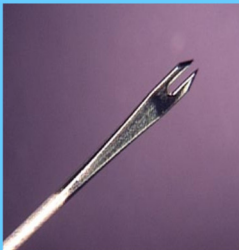
The experiences in a half-dozen clinical trials offer an early look at what military personnel, hospital workers and other emergency workers will likely encounter if Bush adopts the recommendations of his top health advisers to vaccinate as many as 11 million people in the coming months. What is disconcerting, say the people participating in the clinical trials, is that when it comes to smallpox vaccination, what had once been considered ordinary is rather extraordinary by today's standards...[article continues...]

*The Washington Post, Thursday December 5, 2002, A Section, Page A01, By Ceci Connolly, Washington Post Staff Writer



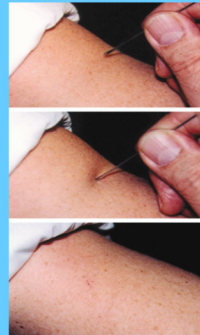


Device Attributes



- Dose sparing: 0.0025 ml held between two tines
- Technique: 10 to 15x microlacerations with blood visible (or not), wide variability tolerable
- Tine tips easily penetrate upper epidermis (through stratum corneum)
- Firm biocompatible metal; (can be flamed multiple times)
- Approximate length 2-3"

Bifurcated Needle



- Invented by Dr. Benjamin Rubin of Wyeth Labs
- Patent No. 3194237 July 13, 1965
- Wyeth waived all royalties for needles manufactured under contract for WHO
- WHO use started 1968

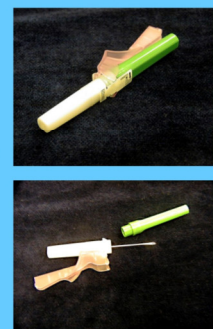
Today's Bifurcated Needle

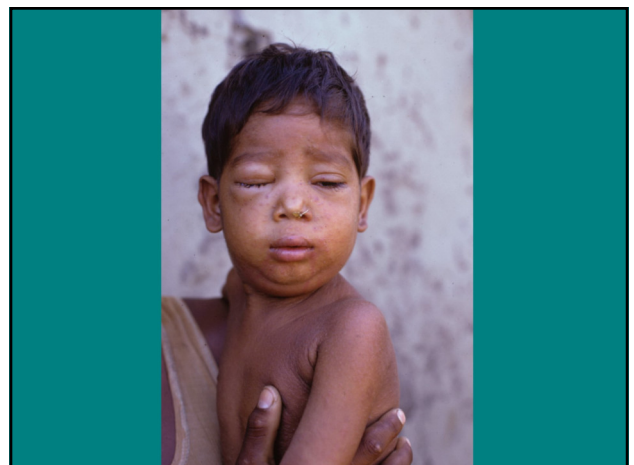
- Classic bifurcated needle
- Individually packaged, sterile, clean, blister wrap
- Hard shield
- Same feel/ size as original
- Back end hub allows for safer handling, especially if dropped. Required for automated assembly
- Dispose using standard sharps container
- FDA 510(k) filing process underway (Dec '01)



Bifurcated Needle - HCW Safety Solution

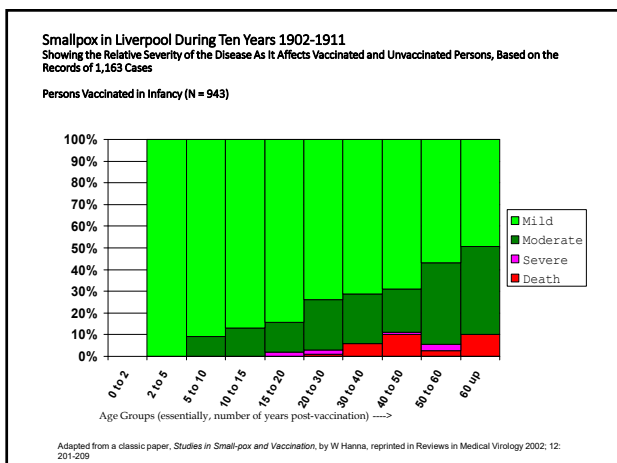
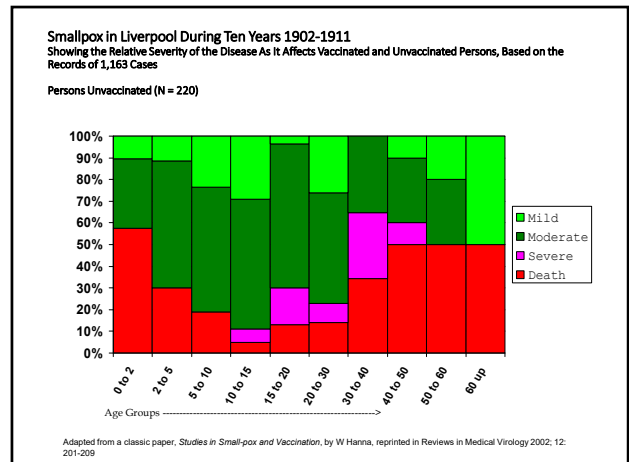
- Use infrastructure from Vacutainer Eclipse safe blood collection system
- Standard device used in U.S.
- Identical bifurcated needle end
- Lowest cost, fastest time to market
- Available June '02







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October 16, 2003 USA Today by Anita Manning

The federal government "Smallpox Vaccination Plan 'Ceased'"

Although no government officials have given the order to stop the sluggishly moving program to vaccinate healthcare and emergency workers against smallpox, Ray Strikas, director of smallpox preparedness and response for the Centers for Disease Control and Prevention's (CDC's) National Immunization Program, acknowledged that the plan has stopped.

The plan originally called for 450,000 healthcare workers to be vaccinated, but the CDC shipped only 291,400 doses to administration centers, and just 38,549 people had actually obtained the vaccine at last count, according to recent figures. At the program's peak, hundreds of people were getting the vaccine each day, but more recently just "a few per week" are seeking the vaccination, according to Strikas.

Even before it began, the vaccination program was questioned by many health groups that expressed concern over the possible side effects of the vaccine, and while most of those side effects have failed to arise, an unexpected risk of heart problems found in April 2003 led to further concern about the vaccine.

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Immunization: let's call it magic

Sir - Prevention in the modern medical sense is not a familiar concept to the majority of the world's population. You can set a boy to prevent the cattle from eating poisonous seeds and you can tell a small girl to watch that the baby does not fall into the well, but sticking needles into the buttock so that in years to come a child will not catch certain diseases is in the realm of magic.

It should be marketed as magic. You catch your enemy, kill him, and eat his heart and liver in order to gain his strength. In the same way you catch hold of a disease, kill it, extract the juice from it, and drink the juice in order to have power over the disease. If there is the juice of several diseases to be drunk, it should be taken at three successive new moons. There should be drums and dancing when the immunization team comes to town.

M. Miles
Rehabilitation Consultant
Mental Health Centre
Mission Hospital, Peshawar, Pakistan

World Health Forum - Volume 5, 1984

"No lesson seems to be deeply inculcated by the experience of life as that you should never trust experts:

If you believe the doctors, nothing is wholesome

If you believe the theologians, nothing is innocent

If you believe the soldiers, nothing is safe

They all require to have their strong wine diluted by a very large admixture of insipid common sense."

Lord Salisbury (1830-1903), from a letter to Lord Lytton, dated 15 June 1877
quoted by Lady Gwendolyn Cecil, *Life of Robert, Marquis of Salisbury*, volume II chapter 4.

14 OCTOBER 2010

Rinderpest virus has been wiped out, scientists say

BY PALLAB GHOSH SCIENCE CORRESPONDENT, BBC NEWS

SCIENTISTS WORKING FOR THE UN SAY THAT THEY HAVE ERADICATED A VIRUS WHICH CAN BE DEADLY TO CATTLE.

IF CONFIRMED, RINDERPEST WOULD BECOME ONLY THE SECOND VIRAL DISEASE - AFTER SMALLPOX - TO HAVE BEEN ELIMINATED BY HUMANS. RINDERPEST WAS ONCE PREVALENT IN THE MIDDLE EAST, AFRICA AND ASIA.

THE UN'S FOOD AND AGRICULTURE ORGANIZATION (FAO) HAS SAID THAT IT WILL NOW SUSPEND ITS EFFORTS TO TRACK AND ELIMINATE THE VIRUS. THE FAO SAID IT WAS CONFIDENT THE VIRUS HAS BEEN ERADICATED FROM THOSE PARTS OF THE WORLD WHERE IT IS PREVALENT.

THE ERADICATION OF THE VIRUS HAS BEEN DESCRIBED AS THE BIGGEST ACHIEVEMENT IN VETERINARY HISTORY AND ONE WHICH WILL SAVE THE LIVES AND LIVELIHOODS OF MILLIONS OF THE POOREST PEOPLE IN THE WORLD.



"Smallpox can, but probably never will be, wholly eradicated. The chief obstacle which stands in the way of its eradication is an inability to recognise facts, and to make the proper deductions from them, which seems to be associated with certain orders of mind. The facts with regard to the production of smallpox immunity by vaccinia are perfectly established. The order of mind which leads to their denial will probably never disappear from the human race."

*Selected Essays on Syphilis and Small-pox,
Translation and Reprints from Various Sources,
W. T. Councilman, 1906
page 189, edited by A. E. Russel
New Sydenham Society, London*

The End